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EXAMINER

BEISNER, WILLIAM H

ART UNIT PAPER NUMBER

1744

DATE MAILED: 05/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/763,077

Applicant(s)

METZLER ET AL.

Examiner

William H. B isner

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-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-31 is/are pending in the application.
- 4a) Of the above claim(s) 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 August 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 16-30, drawn to a bioreactor device, classified in class 435, subclass 297.5.
 - II. Claim 31, drawn to a kit, classified in class 435, subclass 68.1.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions of Group I and Group II are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention of Group II has separate utility such as for use in a membrane device that only include a single well, such as that disclosed in the reference of Kim et al.(Biotechnol. Prog.). See MPEP § 806.05(d).
3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.
4. During a telephone conversation with Kenneth J. Waite on 27 May 2003 a provisional election was made with the preservation for the right to traverse to prosecute the invention of Group I, claims 16-30. Affirmation of this election must be made by applicant in replying to this Office action. Claim 31 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.
5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

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currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Drawings

6. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the all of the claimed elements of the device encompassed by the language of claims 16-30 must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

In response to Applicants' comments concerning this objection, the Examiner is requesting additional drawings that depict the claimed invention. While such drawings are not necessary for the understanding of the invention, 37 CFR 1.83(a) and/or 37 CFR 1.81(c), provide the authority of the Examiner to request drawings of the claimed invention. See M.P.E.P. 608.02.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 16, 17, 24, 25, 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Medicus et al. (US 4,450,076).

The reference of Medicus et al. discloses a dialyzer device which includes an external housing (32) with a cover (44). The device includes an inner housing (40) which includes wells (10) with a cap (18) and a semipermeable membrane (14) separating the interior of the wells (10) with respect to the liquid supply region defined by the external housing (32). The device includes means (52, 48, 36, 34) for moving and incubating the liquids contained on either side of the membranes.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Medicus et al.(US 4,450,076).

The reference of Medicus et al. has been discusses above.

Claims 21 and 22 recite the volume of the well chamber and the volume of the supply chamber with respect to the volume of the well chamber.

While the reference of Medicus et al. is silent as to the specific volumes, the reference is drawn to a "small-sample dialyzer". In the absence of a showing of unexpected results and/or criticality, it would have been obvious to one of ordinary skill in the art to determine the optimum volumes of the chambers based merely on the specifics of the dialysis method to be performed in the device while maintaining the desired efficiency of the system.

13. Claims 21, 22 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Medicus et al.(US 4,450,076) in view of Riley et al.(US 3,623,611).

The reference of Medicus et al. has been discussed above.

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Claim 26 requires that the inner housing be made of a bored blocks with a membrane fixed between two blocks so as to define a plurality of wells with membranes at a bottom of each well.

The reference of Riley et al. discloses that it is known in the art to form a multiple well device wherein the bottom of each well includes a membrane by fixing a membrane between bored blocks (See Figure 3).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to manufacture the inner container of the primary reference in a manner as suggested by the reference of Riley et al. for the known and expected result of providing an alternative means recognized in the art for defining a plurality of wells with a membrane defining the bottom of each well. The technique of the reference of Riley et al. eliminates the need to individually cut each membrane for each well as is required of the primary reference.

With respect to the claimed volumes of claims 21 and 22, the reference of Riley et al. also discloses that it is known to employ sample chambers for dialysis devices with a volume of 0.001ml or less (See the abstract).

In the absence of a showing of unexpected results and/or criticality, it would have been obvious to one of ordinary skill in the art to determine the optimum volumes of the chambers based merely on the specifics of the dialysis method to be performed in the device while maintaining the desired efficiency of the system.

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14. Claims 16, 17, 21, 22, 24, 25, 27, 28, 29 and 30/27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (Biotech. Prog.) in view of Medicus et al. (US 4,450,076).

The reference of Kim et al. discloses a method and device for the performance of biological reactions in a dialysis device (See Figure 4).

The instant claims differ by reciting that the device includes an inner housing with at least two wells.

The reference of Medicus et al. discloses a dialysis device which is known in the art and is similar in construction to that of the device disclosed by the reference of Kim et al. The device of Medicus et al. discloses an inner housing with a plurality of separate sample chambers (See Figure 5). Specifically the reference of Medicus et al. discloses a dialyzer device which includes an external housing (32) with a cover (44). The device includes an inner housing (40) which includes wells (10) with a cap (18) and a semipermeable membrane (14) separating the interior of the wells (10) with respect to the liquid supply region defined by the external housing (32). The device includes means (52, 48, 36, 34) for moving and incubating the liquids contained on either side of the membranes.

In view of this teaching, it would have been obvious to one of ordinary skill in the art to perform the method disclosed by the reference of Kim et al. in a device as disclosed by the reference of Medicus et al. for the known and expected result of providing a device which would allow for a plurality of simultaneous reactions to be performed in a single dialysis system.

Claims 21 and 22 recite the volume of the well chamber and the volume of the supply chamber with respect to the volume of the well chamber.

While the reference of Medicus et al. is silent as to the specific volumes, the reference is drawn to a "small-sample dialyzer". In the absence of a showing of unexpected results and/or criticality, it would have been obvious to one of ordinary skill in the art to determine the optimum volumes of the chambers based merely on the specifics of the dialysis method to be performed in the device while maintaining the desired efficiency of the system.

15. Claims 21, 22, 26 and 30/26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al.(Biotech. Prog.) in view of Medicus et al.(US 4,450,076) and Riley et al.(US 3,623,611).

The combination of the references of Kim et al. and Medicus et al. has been discussed above.

Claim 26 requires that the inner housing be made of a bored blocks with a membrane fixed between two blocks so as to define a plurality of wells with membranes at a bottom of each well.

The reference of Riley et al. discloses that it is known in the art to form a multiple well device wherein the bottom of each well includes a membrane by fixing a membrane between bored blocks (See Figure 3).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to manufacture the inner container of the primary reference in a manner as suggested by the reference of Riley et al. for the known and expected result of providing an alternative means recognized in the art for defining a plurality of wells with a membrane defining the bottom of each well. The technique of the reference of Riley et al.

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eliminates the need to individually cut each membrane for each well as is required of the primary reference.

With respect to the claimed volumes of claims 21 and 22, the reference of Riley et al. also discloses that it is known to employ sample chambers for dialysis devices with a volume of 0.001ml or less (See the abstract).

In the absence of a showing of unexpected results and/or criticality, it would have been obvious to one of ordinary skill in the art to determine the optimum volumes of the chambers based merely on the specifics of the dialysis method to be performed in the device while maintaining the desired efficiency of the system.

16. Claims 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al.(Biotech. Prog.) in view of Medicus et al.(US 4,450,076) and Alakhov et al.(US 5,478,730).

The combination of the references of Kim et al. and Medicus et al. has been discussed above.

While the reference of Kim et al. discloses the use of a semipermeable membrane the reference is silent as to the pore size of the membrane.

The reference of Alakhov et al. discloses that when performing a polypeptide synthesis as disclosed by the reference of Kim et al. it is known in the art to employ a semipermeable membrane with a pore size of 100kD or less (See column 4, lines 38-52).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ a membrane of a pore size which is known in the art (100kD or less) for the control of reactants and products in the dialysis system.

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17. Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al.(Biotech. Prog.) in view of Medicus et al.(US 4,450,076) and Rothschild et al.(US 5,948,624).

The combination of the references of Kim et al. and Medicus et al. has been discussed above.

The above claims differ by reciting that the wells are coated with streptactin, avidin or streptavidin.

The reference of Rothschild et al. discloses that it is known in the art to immobilize avidin or streptavidin on a solid surface (microtiter wells) so as to isolate chemical, biochemical or biological materials (See column 18, lines 57-67).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the wells of the modified primary reference with immobilized avidin or streptavidin for the known and expected result of providing a means recognized in the art for purification of the polypeptide product produced by the dialysis reaction.

Response to Arguments

18. Applicant's arguments filed 19 March 2003 have been fully considered but they are not persuasive.

With respect to the rejection of claims 16, 17, 24, 25, 27 and 28 over the reference of Medicus et al. under 35 USC 102(b), Applicants argue that the rejection is improper because claim 16 as originally submitted clearly requires that the wells of the inner housing contain a

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producing system. Applicants point out that the reference of Medicus et al. is silent as to the presence of “a producing system”.

In response, the Examiner is of the position that the rejection is proper because claim 16 does not positively recite that the wells of the inner housing contain a producing system. The language of claim 16 as originally filed recites “wherein the wells of the inner housing each contain a producing system **during the biochemical reaction**”. This claim language is interpreted to mean that the when **using** the device the wells contain a producing system. As a result, the structure of the reference of Medicus et al. is considered to meet the structure of the claimed device. Note the structure of Medicus et al. is capable of being used for carrying out biochemical reaction and statements of intended use carry no patentable weight in apparatus-type claims.

With respect to the rejection of claims 21 and 22 over the reference of Medicus et al. under 35 USC 103, Applicants argue that the reference of Medicus et al. fails to disclose the claimed producing system.

These arguments are not persuasive for the same reasons as set forth above with respect to the 35 USC 102 rejection.

With respect to the rejection of claims 21, 22 and 26 over the reference of Medicus et al. in view of Riley et al. under 35 USC 103, Applicants argue that the reference of Riley additionally fails to disclose the claimed producing system.

In response, as stated previously, the instant claim language does not positively recite the producing system as an element of the claimed device.

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With respect to the rejection of claims 16, 17, 21, 22, 24, 25, and 27-30 over the reference of Kim et al. in view of Medicus et al., Applicants argue that the combination is improper because neither of the references indicates the desirability of such a combination. Applicants stress that the Examiner has employed improper "hind sight" examination by combining the references. .

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In the instant application, the reference of Kim et al. clearly discloses performing the protein synthesis in a small-sample dialyzer as shown in Figure 4. The device of Medicus et al. is also a small-sample dialyzer. The device of Medicus et al. can include a single well inner housing or a multiple well inner housing (See Figures 5 and 7). The reference of Medicus et al. also discloses improving the dialysis process by agitating both of the liquids on either side the membrane (See column 1, lines 42-49). In view of these disclosures, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the device of the reference of Medicus et al. to perform the method of Kim et al. in view of the accelerated dialysis provided by the design of the device of the Medicus et al. over the device of the Kim et al. device. The structure of the device of the Medicus et al. reference also provides for the

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processing of multiple samples which is also advantageous for the known and expected result of allowing multiple samples to be processed simultaneously. Furthermore, it is well established that mere duplication of parts has no patentable significance unless a new and unexpected result is produced (See *In re Harza*, 124 USPQ 378 (CCPA 1960)).

With respect to the rejection of claims 18-23, 26 and 30 over the combination of the references of Kim et al. and Medicus et al. taken further in view of the references of Riley et al., Alakhov et al. or Rothschild, Applicants argue that none of the references of Riley et al., Alakhov et al. or Rothschild cure the deficiencies recited previously concerning the combination of the references of Kim et al. and Medicus et al.

In response, the references of Riley et al., Alakhov et al. and Rothschild were cited to address additional claim limitations and were not relied upon to provide the motivation for combining the references of Kim et al. and Medicus et al. As stated previously, the Examiner is of the position that the combination of the references of Kim et al. and Medicus et al. is proper and does not involve impermissible hindsight.

Conclusion

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period


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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 703-308-4006. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:40am to 4:10pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 703-308-2920. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9310 for regular communications and 703-872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.


William H. Beisner
Primary Examiner
Art Unit 1744

WHB
May 27, 2003